1614

Attorney's Docket No. 018995-452

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	
Nishizumi NISHIMUTA et al.	Group Art Unit: 1614
Application No.: 10/046,575	Examiner: Vickie Y. Kim
Filed: January 16, 2002	Confirmation No.: 4939
For: EXTERNAL PREPARATION FOR SKIN DISEASES CONTAINING NITROIMIDAZOLE	

AMENDMENT AND REPLY TRANSMITTAL LETTER

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Enclosed is an Amendment and Reply for the above-identified patent application.

[ ] A Petition for Extension of Time is also enclosed.

[ ] A Terminal Disclaimer and the [ ] $55.00 (2814) [ ] $110.00 (1814) fee due under 37 C.F.R. § 1.20(d) are also enclosed.

[ ] Also enclosed is/are _____.

[ ] Small entity status is hereby claimed.

[ ] Applicant(s) requests continued examination under 37 C.F.R. § 1.114 and enclose the [ ] $385.00 (2801) [ ] $770.00 (1801) fee due under 37 C.F.R. § 1.17(e).

[ ] Applicant(s) requests that any previously unentered after final amendments not be entered. Continued examination is requested based on the enclosed documents identified above.

[ ] Applicant(s) previously submitted ___, on ___, for which continued examination is requested.

[ ] Applicant(s) requests suspension of action by the Office until at least ___, which does not exceed three months from the filing of this RCE, in accordance with 37 C.F.R. § 1.103(c). The required fee under 37 C.F.R. § 1.17(i) is enclosed.

[ ] A Request for Entry and Consideration of Submission under 37 C.F.R. § 1.129(a) (1809/2809) is also enclosed.

[ ] No additional claim fee is required.

[ ] An additional claim fee is required, and is calculated as shown below:

AMENDED CLAIMS					
	NO. OF CLAIMS	HIGHEST NO. OF CLAIMS PREVIOUSLY PAID FOR	EXTRA CLAIMS	RATE	ADD'L FEE
Total Claims	30	MINUS 31 =		× $18.00 (1202) =	-0-
Independent Claims	1	MINUS 3 =		× $86.00 (1201) =	-0-
If Amendment adds multiple dependent claims, add $290.00 (1203)					
Total Claim Amendment Fee					
If small entity status is claimed, subtract 50% of Total Claim Amendment Fee					
TOTAL ADDITIONAL CLAIM FEE DUE FOR THIS AMENDMENT					-0-

[ ] A total fee in the amount of $ _____ is enclosed.

[ ] Charge $_____ to Deposit Account No. 02-4800.

The Director is hereby authorized to charge any appropriate fees under 37 C.F.R. §§ 1.16, 1.17, 1.20(d) and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800. This paper is submitted in duplicate.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

Date: October 16, 2003

By: _____
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AMENDMENT AND REPLY

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Official Action mailed July 16, 2003, Applicants herein provide the following amendments and remarks.

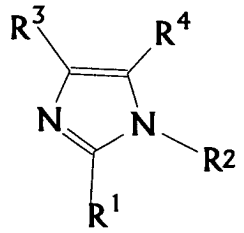
AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

Claim 1 (currently amended): A method of therapeutically treating, prophylactically treating or ameliorating ~~skin disease~~ atopic dermatitis which comprises applying to portions of the disease of a patient an external preparation comprising

a nitroimidazole derivative represented by the following formula (I), a pharmaceutically acceptable salt thereof, an ester thereof or other derivatives thereof as an active ingredient:



(I)

wherein R^1, R^3 and R^4 may be the same or different and each independently represents a hydrogen atom, a nitro group, a lower alkyl group, a lower alkyl group substituted by 1 or more substituents which may be the same or different selected from Substituent group α and Substituent group β, a lower alkenyl group, or a lower alkenyl group substituted by 1 or more substituents which may be the same or different selected

from the Substituent group α and the Substituent group β; and R^2 represents a hydrogen atom, a lower alkyl group, a lower alkyl group substituted by 1 or more substituents which may be the same or different selected from the Substituent group α and the Substituent group β, a lower alkenyl group or a lower alkenyl group substituted by 1 or more substituents, which may be the same or different selected from the Substituent group α and the Substituent group β,

provided that any one of R^1, R^3 and R^4 is a nitro group, ~~wherein. The~~ wherein the Substituent group α comprises a lower alkyloxy group, a lower alkyloxy group substituted by 1 or more substituents which may be the same or different selected from the Substituent group β, a lower alkylcarbonyloxy group, a lower alkylcarbonyloxy group substituted by 1 or more substituents which may be the same or different selected from the Substituent group β, a lower alkylsulfonyl group, a lower alkylsulfonyl group substituted by 1 or more substituents which may be the same or different selected from the Substituent group β, a cycloalkyl group, a cycloalkyl group substituted by 1 or more substituents which may be the same or different selected from the Substituent group β, a heteroaryl group, a heteroaryl group substituted by 1 or more substituents which may be the same or different selected from the Substituent group β, an aryl group and an aryl group substituted by 1 or more substituents which may be the same or different selected from the Substituent group β; and

the Substituent group β comprises a hydroxy group, a mercapto group, a halogen atom, an amino group, a lower alkylamino group, a lower alkyloxy group, a lower alkenyl

group, a cyano group, a carboxy group, a carbamoyloxy group, a carboxyamide group, a thiocarboxyamide group and a morpholino group.

Claim 2 (original): The method of claim 1, wherein R^4 is a nitro group.

Claim 3 (original): The method of claim 2, wherein R^1 and R^2 are the same or different and represent a lower alkyl group, a lower alkyl group substituted by 1 or more substituents selected from the Substituent group α and the Substituent group β, a lower alkenyl group, or a lower alkenyl group substituted by 1 or more substituents which may be the same or different selected from the Substituent group α and the Substituent group β, and R^3 is a hydrogen atom.

Claim 4 (withdrawn): The method of claim 3, wherein the Substituent group α is a lower alkyloxy group and the Substituent group β is a hydroxy group, an amino group, a halogen atom, a cycloalkyl group, a heteroaryl group or an aryl group.

Claim 5 (withdrawn): The method of claim 4, wherein the Substituent group β is a hydroxy group, an amino group, a halogen atom or a heteroaryl group.

Claim 6 (currently amended): The method of claim ~~5~~ 4, wherein R^1 is a lower alkyl group.

Claim 7 (withdrawn): The method of claim 5, wherein R^2 is a lower alkyl group substituted by a hydroxy group.

Claim 8 (withdrawn): The method of claim 1, wherein the preparation comprises 2-(2-methyl-5-nitroimidazole-1-yl)ethanol (general name: metronidazole), a pharmaceutically acceptable salt thereof, an ester thereof or other derivatives thereof as an active ingredient.

Claim 9 (original): The method of claim 3, wherein the Substituent group α is a lower alkylsulfonyl group or a lower alkylsulfonyl group substituted by substituents which may be the same or different selected from the Substituent group β and the Substituent group β is a hydroxy group, a halogen atom, an amino group, a lower alkylamino group, a lower alkyloxy group, a lower alkenyl group, a cyano group, a carboxy group, a cycloalkyl group or an aryl group.

Claim 10 (original): The method of claim 9, wherein R^1 is a lower alkyl group or lower alkyl group substituted by substituents which may be the same or different selected from the Substituent group β.

Claim 11 (original): The method of claim 9, wherein R^2 is a lower alkylsulfonyl group or a lower alkylsulfonyl group substituted by substituents which may be the same or different selected from the Substituent group β.

Claim 12 (original): The method of claim 1, wherein the preparation comprises 1-(2-ethylsulfonylethyl)-2-methyl-5-nitroimidazole (general name: tinidazole) or a pharmaceutically acceptable salt thereof as an active ingredient.

Claim 13 (original): The method of claim 1 which comprises applying one compound of the nitroimidazole derivatives as defined in claim 1 and one medicine selected from the group consisting of an antimycotic agent, antibacterial agent, sulfa, immunosuppressant, antiinflammatory agent, antibiotic, antiviral agent, metabolic antagonist, antihistamine, tissue repair promoter, vitamin, antiallergic, local anesthetic, hair agent and steroid simultaneously or separately with an interval to the portions.

Claim 14 (original): The method of claim 13, wherein the antimycotic agent, the antibacterial agent, the sulfa, the immunosuppressant, the antiinflammatory agent, the antibiotic, the antiviral agent, the metabolic antagonist, the antihistamine, the tissue repair promoter, the vitamin, the antiallergic, the local anesthetic, the hair agent or the steroids is used with a concentration at which the agent itself does not demonstrate any pharmacological effect.

Claim 15 (withdrawn): The method of claim 1 wherein the preparation further comprises crotamiton.

Claim 16 (Canceled).

Claim 17 (withdrawn): The method of Claim 1, wherein the skin disease is facial atopic dermatitis.

Claim 18 (withdrawn): The method of claim 1, wherein the skin disease is infant atopic dermatitis.

Claim 19 (withdrawn): The method of claim 1, wherein the skin disease is blotches, pigmentation or scars of the skin.

Claim 20 (withdrawn): The method of claim 1, wherein the skin disease is psoriasis.

Claim 21 (withdrawn): The method of claim 1, wherein the skin disease is hircus, body odor or osmidrosis.

Claim 22 (withdrawn): The method of claim 1, wherein the skin disease is contact dermatitis, plant dermatitis or insect bites.

Claim 23 (withdrawn): The method of claim 1, wherein the skin disease is dermal pruritis or drug rash.

Claim 24 (withdrawn): The method of claim 1, wherein the skin disease is chilblain.

Claim 25 (withdrawn): The method of claim 1, wherein the skin disease is erythroderma.

Claim 26 (withdrawn): The method of claim 1, wherein the skin disease is tinea.

Claim 27 (withdrawn): The method of claim 1, wherein the skin disease is suppurative skin disease.

Claim 28 (withdrawn): The method of claim 1, wherein the skin disease is pressure sore.

Claim 29 (withdrawn): The method of claim 1, wherein the skin disease is wound.

Claim 30 (withdrawn): The method of claim 1, wherein the skin disease is palmoplantar pustulosis, lichen planus, lichen nitidus, pityriasis rubra pilaris, pityriasis rosea, erythema (including polymorphic exudative erythema, erythema nodosum and Darier's erythema annulare centrifugum), discoid lupus erythematosus, drug rash and toxic rash, alopecia areata, burns (including scars and keloids), pemphigus, Duhring dermatitis herpetiformus (including pemphigoid), seborrheic dermatitis, dermal stomatitis, Candidiasis (including interdigital erosion, intertrigo, dermal Candidiasis, infantile parasitic erythema, perionychia and vaginal Candidiasis) or tinea versicolor.

Claim 31 (original): The method of claim 1 wherein a concentration of the nitroimidazole derivative is 0.1 to 20 % by weight based on the amount of the preparation.